UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,337	12/09/2005	Valerio Cioli	BUG5-39170	2541

116 7590 12/03/2008

PEARNE & GORDON LLP
1801 EAST 9TH STREET
SUITE 1200
CLEVELAND, OH 44114-3108

EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
12/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,337	CIOLI, VALERIO	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 - 21* is/are pending in the application.

4a) Of the above claim(s) *14 - 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 - 13, 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/18/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed September 18, 2008, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Response to Amendment

1. The declaration under 37 CFR 1.132 filed September 18, 2008 is insufficient to overcome the rejection of claims 11 – 13 under 35 USC 102(b) based on Kerouac et al. (WO 99/40898) and claims 11 – 13 and 21 under 35 USC 103(a) based upon Kerouac et al (WO 99/40898) and Mehta (WO 01/85134) as set forth in the last Office action because: the declaration is not commensurate in scope with the claims and does not represent a comparison of the claims to the closest prior art.

The declaration provides information regarding sublingual formulation of one non-steroidal anti-inflammatory agent FANS, nimesulide, and an oral formulation of the same active ingredient but a higher dosage (100 mg for the oral dosage form vs 25 and 50 mg for the sublingual dosage). The maximum blood concentration was achieved in a shorter period of time for the sublingual administration form (¶ 5).

No information was given on the other ingredients present in either the sublingual or oral formulation and how this data applies to the compositions prepared in the cited prior art. No mention of other non-steroid anti-inflammatory FANS agents are mentioned

in the declaration. The claims contain a functional limitation of the sublingual formulation has a therapeutic dose which is "reduced in comparison with the therapeutic dose of the same anti-inflammatory agent in a pharmaceutical formulation for oral administration, which provides the same therapeutic effect of treatment of inflammatory symptoms." While the declaration demonstrated that the sublingual formulations reach the peak level in the blood in a shorter period of time (decreased t_{max}), the reference oral formulation could also be said to have an improved therapeutic effect with a longer duration of therapeutic effect as measurable blood levels of the active ingredient persist for 8 hours instead of 2.5 hours for the sublingual formulation.

Claim Rejections - 35 USC § 112 – 1st Paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 11 – 13 and 21 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The full genus of "inflammatory symptoms" did not meet the written description provision. This rejection is MAINTAINED

for the reasons of record set forth in the Office Action mailed April 22, 2008 and those set forth below.

Applicant has amended to independent claim 11 but none of the remarks in the section of the Office Action deal with the written description rejection.

This rejection is maintained as the genus of "inflammatory symptoms" is still present in the claims and Applicant has not argued or provided evidence that the full genus of "inflammatory symptoms" is supported by the application as filed.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 11 – 13 and 21 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because it was unclear if the instant claims were drawn to a method of administering a dosage form or a method of treating inflammatory symptoms. This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 22, 2008 and those set forth below.

Applicant has not amended the preamble of the claim or added an active step of administering a dosage form to clarify what type of method is being claimed. In the brief section of the remarks dealing with all of the rejections under 35 USC 112, no

comments regarding this particular rejection were made. Therefore, this rejection is maintained.

6. Claims 11 – 13 and 21 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because of the phrase it was unclear what was meant by “therapeutic effect". This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 22, 2008 and those set forth below.

Applicant has amended the claims to read “same therapeutic effect of treatment of inflammatory symptoms”.

This amendment does not fully address the rejections and the claims remain vague and indefinite. It is still unclear by what aspect(s) of the therapeutic effect is/are being measured. "Therapeutic effect” could relate to how long it takes for symptom relief to begin (t_{max}), the total length of time the symptoms are treated or the overall efficacy of all the inflammatory symptoms which are being treated. Applicant has also not explained how the capsules and pill forms of the sublingual dosage form, forms which are generally classified as oral dosage forms, are different from the oral dosage form used in the comparison. Taken together, one of skill in the art cannot define the standard by which the reduced dosage for the same therapeutic effect is determined so this rejection is maintained.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 11 – 13 were rejected under 35 U.S.C. 102(b) as being anticipated by Kerouac et al. (WO 99/40898). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 22, 2008 and those set forth below.

Applicant traverses this rejection in part by the submission of a Rule 1.132 declaration which was discussed above. Applicant has also argued the Kerouac et al. does not disclose that the therapeutic dose of the anti-inflammatory agent is reduced in comparison with the therapeutic dose of the same anti-inflammatory agent in a pharmaceutical formulation for oral administration and that the oral and sublingual dosage form contain the same dosage of active principle. Therefore, Kerouac et al. does not solve the problem of a sublingual formulation that can give a quick therapeutic effect while avoiding the drawbacks of oral administration, as such as gastrointestinal damage, stomach pain and partial elimination through the liver. The results are surprising and unexpected as the combination of the desired therapeutic effect and low side effects can be achieved though reducing the standard oral dosage from with a sublingual formulation. Both the oral and sublingual formulation need higher dosages of

the active ingredient to achieve the desired therapeutic effect as at least part of the active ingredient is orally absorbed.

These arguments are not found to be persuasive. Unexpected results are not germane to a rejection under 35 USC 102 (MPEP 2131.04). The compositions of Kerouac et al. contain a portion of the dose which is absorbed sublingually, while the remainder is absorbed by other routes (buccal or gastrointestinal) (p 5, ln 15 – 23). The claims of the instant application do not contain an active step of administering and use the open language of “comprising” so a portion of the dosage form being administered by another route is not excluded. Therefore, the dosage that is administered by the sublingual route is less than the full dosage provided in the dosage form and therefore even when the total amount of active ingredient in the sublingual dosage form of Kerouac et al. as compared to an oral administration form, the dosage which is administered sublingually is less that the standard, while providing the same or increased therapeutic effect (by virtue of the faster onset and some of the dosage form being administered sublingually and thus avoiding a liver first-pass metabolism effect from intestinal absorption of the active ingredient). As discussed above, Applicant has not sufficiently defined the standard by which the comparison is made and the exemplified advantages are inherent to the sublingual dosage route, which are taught by or inherent to (such as the eimiation of a liver first pass metabolism because of the sublingual administration) the compositions of Kerouac et al.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 11 – 13 and 21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kerouac et al. in view of Mehta et al. (WO 01/85134). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 22, 2008 and those set forth below.

Applicant traverses this rejection on the basis that Mehta et al. does not disclose a method of administering a sublingual pharmaceutical formulation but rather buccal cavity administration. The bottom of the tongue (sublingual) and upper part of the tongue and buccal cavity have different blood supplies, which alters the required bioavailability, absorption speed, required dosage and therapeutic effect rendering the

subject matter novel over Mehta et al. The buccal formulation comprises the same amount of active ingredient as an oral composition.

Applicant traverses this rejection in part by the submission of a Rule 1.132 declaration which was discussed above. Applicant has also argued the Kerouac et al. does not disclose that the therapeutic dose of the anti-inflammatory agent is reduced in comparison with the therapeutic dose of the same anti-inflammatory agent in a pharmaceutical formulation for oral administration and that the oral and sublingual dosage form contain the same dosage of active principle. Therefore, Kerouac et al. does not solve the problem of a sublingual formulation that can give a quick therapeutic effect while avoiding the drawbacks of oral administration, as such as gastrointestinal damage, stomach pain and partial elimination through the liver. The results are surprising and unexpected as the combination of the desired therapeutic effect and low side effects can be achieved though reducing the standard oral dosage from with a sublingual formulation. Both the oral and sublingual formulation need a higher dosage of active ingredient to achieve the desired therapeutic effect as at least part of the active ingredient is orally absorbed.

These arguments are not found to be persuasive. A rejection under 35 USC 102 using Mehta et al. was not made so those arguments are moot. Arguments in regards to the decreased sublingual dosage have been laid out in more detail above in the section regarding the 35 USC 102(b) rejection over Kerouac et al. As Mehta et al. is as the secondary reference relied upon to teach the administration of the non-steroidal anti-inflammatory agent nimesulide by a non-gastrointestinal administration mode, the failure

of Mehta et al. to teach buccal but not sublingual administration is not relevant. The unexpected and surprising results of desired therapeutic effects and low side effects can be achieved by reducing the standard oral dosage of active principle achieved in a quicker manner than oral administration are known and therefore not unexpected. Kerouac et al. discloses that sublingual absorption results in more rapid onset of action of the therapeutic agent (abstract).

Decreased gastrointestinal symptoms or side effects are not explicitly claimed by Applicant. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., liver metabolism, decreased side effects) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Rather, the claims recite the same therapeutic effect is being achieved by a reduced sublingual dose.

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. This application contains claim14 – 20 drawn to an invention nonelected with traverse in the reply filed on February 7, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW